Declaration of Jeffrey Schlom

I, Jeffrey Schlom, declare and state:

(1) I am a co-inventor of the inventions disclosed and claimed in U.S. Patent No. 09/856,988, filed May 30, 2001 ("the application").

(2) A copy of my curriculum vitae is attached.

(3) I have reviewed the Office Action dated May 18, 2004 in the application and understand that the Examiner believes the claimed invention is anticipated by U.S. Patent No. 6,548,068 ("the '068 patent) and that the claims are obvious over claims 1-6 of the '068 patent.

(4) I believe the invention of claim 37 is a host cell comprising a recombinant vector comprising nucleic acid sequences encoding a combination of B7-1, ICAM-1 and LFA-3 and that the '068 patent does not describe this specific combination.

(5) I also believe that this specific combination of B7-1, ICAM-1 and LFA-3 is not suggested by the claims in the '068 patent. Moreover, even if one were to select B7-1, ICAM-1 and LFA-3 from those co-stimulatory molecules recited in the claims of the '068 patent, no one could have predicted the surprising results obtained using nucleic acid sequences encoding those three specific co-stimulatory molecules.

(6) The application (example 27a-d) describes studies performed using an in vitro assay. These studies demonstrate the unexpected synergy that results when B7-1, ICAM-1 and LFA-3 are all combined (designated TRICOM) to enhance the activity of isolated CD4 T cells or isolated CD8 T cells. Particular attention should be paid to the point that the sum of the activity seen by each one of these costimulatory molecules used alone, is far exceeded when used in combination. It should also be pointed out that even the combination of B7-1 and ICAM-1 is very much inferior to the combination in TRICOM (example 27a-d).

(7) These results, as set forth in the attached graph (Exhibit 1) showed that B7-1, ICAM-1 and LFA-3 worked together in a synergistic way to enhance an immune response, *i.e.* T-cell proliferation. This finding was unexpected.

(8) Other work from my laboratory shows that one cannot predict which combination of costimulatory molecules might have a synergistic effect. In fact, it is not clear that all combinations of costimulatory molecules will have an additive effect. For instance, as seen in Figure 1 (Exhibit 2) the addition of a fourth costimulatory molecule (CD70) to TRICOM actually inhibits the activation of T cells as compared to the use of TRICOM alone. Another striking example of how one cannot predict the activity seen

with the use of multiple costimulatory molecules is shown in Figure 2 (Exhibit 3). Here it is seen that 4-1BBL is clearly a costimulatory molecule when used alone (left panel). However, when 4-1BBL is used in combination with TRICOM, the activation of T cells is decreased as compared to the use of TRICOM alone (right panel).

(9) These results, as set forth in Exhibit 1-3, strongly support the argument that the results obtained using a recombinant vector comprising nucleic acid sequences encoding B7-1, ICAM-1 and LFA-3 were surprising and unpredictable.

All statements herein are made upon my own knowledge and are true. I understand that willful false statements and the like are punishable by fine or imprisonment, or both (18 USC 1001) and may jeopardize the validity of the application or any patent issuing therefrom.

8-17-04
Date

Jeffrey Schlom, Ph.D.

CURRICULUM VITAE

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Education:

1969	Ph.D. Rutgers University, Waksman Institute, New Brunswick, New Jersey
1966	M.S. Adelphi University, Garden City, New York
1964	B.S. Ohio State University, Columbus, Ohio

Chronology of Employment:

1982 - present	Chief, Laboratory of Tumor Immunology and Biology, Center for Cancer Research, National Cancer Institute (NCI), National Institutes of Health (NIH), Bethesda, MD
2001-present	Professor (Adjunct) of Immunology, School of Medicine and Health Sciences, George Washington University, Washington, D.C.
1996 - present	Member, George Washington University Institute for Biomedical Sciences, Washington, D.C.
1973 - present	Professor (Adjunct), Graduate Faculty in Genetics, George Washington University, Washington, D.C.
1980 - 1982	Chief, Experimental Oncology Section, Laboratory of Cellular and Molecular Biology, Division of Cancer Cause and Prevention, NCI, NIH, Bethesda, MD
1976 - 1980	Head, Tumor Virus Detection Section, Laboratory of Viral Carcinogenesis, Division of Cancer Cause and Prevention, NCI, NIH, Bethesda, MD
1973 -1976	Chairman, Breast Cancer Virus Segment, NCI, NIH, Bethesda, MD
1971 - 1973	Assistant Professor, Department of Human Genetics and Development, College of Physicians and Surgeons of Columbia University, New York, NY
1969 - 1970	Instructor, Department of Human Genetics and Development, College of Physicians and Surgeons of Columbia University, New York, NY

Honors and Other Special Scientific Recognition:

NIH Merit Award, 2002
Highly Cited Researcher in the World (ISI®) in Clinical Medicine
Member, Senior Executive Service, U.S. Public Health Service
Member, World Meeting of University Professors, Jubilee of Universities, The Vatican, Rome, 2000
Special Lecturer, Japanese Society for Surgical Cancer Immunology, Wakayama, Japan, 2000
Distinguished Lecturer, American College of Physicians, 1998
NIH Federal Technology Transfer Award, 1994, 1996, 1997, 1998, 1999, 2000
Turin University Distinguished Scientist Award, 1996
Memorial Sloan Kettering Cancer Center, Frederick S. Philips Memorial Lecture, 1996
The Eighth Apffel Memorial Lecture, Boston Cancer Research Association and the Cancer Research Institute of The New England Deaconess Hospital, 1993
Society for Biological Therapy Award (Laboratory) for Best Paper, 1991, 1992
National Institutes of Health Directors Award, 1988
American Society of Cytology Guest Lectureship Award, 1987
The Rosenthal Foundation Award (American Association for Cancer Research), 1985
Canadian Cancer Society, Distinguished Lecturer for 1985
George Gross Memorial Lecture, Newark Beth Israel Medical Center, 1983
The Leona Kopman Memorial Award, AMC Cancer Research Center, Presented at the International Association for Breast Cancer Research and Treatment, 1983
National Cancer Institute Equal Opportunity Special Achievement Award, 1983
American Cancer Society, Certificate of Appreciation, 1983
Grace Faillace Memorial Lecture, Symposium on the Biologic Control of Human Cancer, 1982
National Institutes of Health Director's Award, 1977

Technology Transfer:

Over 20 patents have either been issued or are pending in the areas of vaccines and monoclonal antibodies.

Current Editorial Board and Committee Memberships:

Member, International Society of Biological Therapy of Cancer
Member, Urologic Oncology Steering Committee, CCR, NCI
Member, Blue Ribbon Panel on Bioterrorism, NIH
Member, Smallpox Vaccine and Attenuated Vaccine Interagency Committee, DHHS
Member, Molecular Targets Faculty Steering Committee, CCR, NCI
Member, Immunology Faculty Steering Committee, CCR, NCI
Member, Steering Committee, Vaccine Working Group, CCR, NCI
Member, Advisory Board, Institute of Human Virology, Baltimore, Maryland
Member, Advisory Board (Adjunct), Karmanos Cancer Center, Detroit, Michigan
Member, Vaccine Research Center Search Committee
Editorial Board, Breast Cancer Research
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